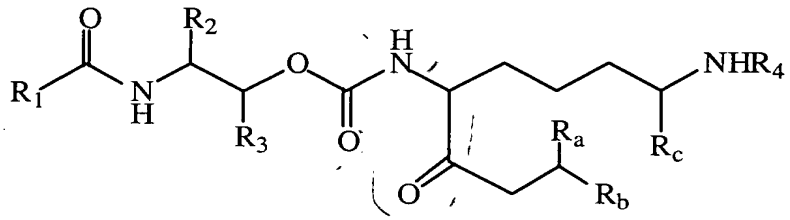
CLAIMS

1. A method of treating solid tumor in a mammal which comprises administering to said mammal an effective amount of a combination of a bioresponse modifier and a chemotherapeutic agent.

2. The method according to claim 1, wherein the bioresponse modifier is a cytokine inducer.

3. The method according to claim 2, wherein the chemotherapeutic agent is a microtubular agent or a macrophage activating agent.

4. The method according to claim 3, wherein the cytokine inducer is a compound of formula I, having the structure



I

wherein

R_1 is selected from the group consisting of hydrogen, a substituted or unsubstituted (C_1-C_{20}) alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkylalkyl group, a vinyl group, an acetylene group, a substituted or unsubstituted amino group, a substituted or unsubstituted acylamino group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aralkylgroup, a substituted or unsubstituted aryloxy group, a substituted or unsubstituted alkoxyaryl group, a substituted or unsubstituted alkoxyaralkyl group and a substituted or unsubstituted monocyclic or bicyclic heterocyclic group containing from 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms;

R_a and R_3 are independently selected from hydrogen, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkoxyaralkyl, vinyl, acetylene and a sustituted or unsubstituted monocyclic or bicyclic heterocycle containing from 1 to 4 heteroatoms selected from the group consisting of nitrogen, sulfur and oxygen atoms provided that, in the case of R_3, the hetero atoms in said heterocycle are not directly bonded to the --CH-- group of the --CH--X-- moiety;

R_2, R_b and R_c are independently selected from carboxy or protected carboxy, carboxy or protected carboxyloweralkyl and carboxyamide;

X is oxygen or nitrogen;

R_4 is H or an amino protecting group; wherein the substituents in the aforementioned substituted alkyl, cycloalkyl, cycloalkylalkyl, amino, acylamino, aryl, aralkyl, aryloxy, alkoxyaryl, alkoxyaryalkyl and heterocyclic groups are selected from the group consisting of halogen, hydroxyl, lower alkyl, lower alkoxy, aryloxy, aralkyloxy, amino, mono- or di-loweralkylamino, arylamino, aralkylamino, carboxyl, formyl, lower alkoxycarbonyl, aryloxycarbonyl, aralkyloxycarbonyl, loweralkylthio, arylthio, aralkylthio, arylsulfinyl, arylsulfinyl, aralkylsulfinyl, lower alkylsulfonyl, arylsulfonyl, aralkylsulfonyl and a monocyclic or bicyclic heterocyclic group having 1- 4 hetero atoms selected from nitrogen, sulfur and oxygen;

or a pharmaceutically acceptable salt thereof.

5. The method according to claim ~~4,~~ in which the compound of formula I is [R-(R*,R*)]-N-[(R)-6-carboxy-N^2-[[2-carboxy-1-methyl-2-[(1-oxoheptyl)amino]ethoxy] carbonyl]-L-lysyl]-alanine or a pharmaceutically acceptable salt thereof.

6. The method according to claim 5 wherein the microtubular agent or macrphage activating agent is selected from the group consisting of paclitaxcel, docetaxel, vincristine, vinblastine, vinorelbine, adriamycin, doxirubicin, cisplatin, carboplatin, mitomycin C, and bleomycin.

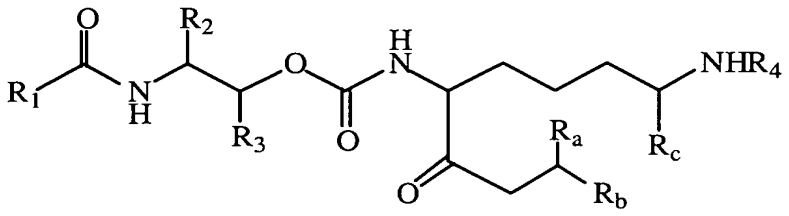
7. The method according to claim 6, wherein the microtubular agent or macrophage activating agents are paclitaxcel and carboplatin.

8. A method of potentiating the effects of a chemotherapeutic regimen in a mammal in need of treatment with such regimen which comprises administering a bioresponse modifier in addition to a chemotherapeutic regimen.

9. The method according to claim 8, wherein the bioresponse modifier is a cytokine inducer.

10. The method according to claim 9, wherein the chemotherapeutic agent is a microtubular agent or a macrophage activating agent.

11. The method according to claim 10, wherein the cytokine inducer is a compound of formula I, having the structure



I

wherein

R_1 is selected from the group consisting of hydrogen, a substituted or unsubstituted (C_1-C_{20}) alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkylalkyl group, a vinyl group, an acetylene group, a substituted or unsubstituted amino group, a substituted or unsubstituted acylamino group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aralkylgroup, a substituted or unsubstituted aryloxy group, a substituted or unsubstituted alkoxyaryl group, a substituted or unsubstituted alkoxyaralkyl group and a substituted or unsubstituted

monocyclic or bicyclic heterocyclic group containing from 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur and oxygen atoms;

R_a and R_3 are independently selected from hydrogen, substituted or unsubstituted (C_1-C_6) alkyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkoxyaralkyl, vinyl, acetylene and a sustituted or unsubstituted monocyclic or bicyclic heterocycle containing from 1 to 4 heteroatoms selected from the group consisting of nitrogen, sulfur and oxygen atoms provided that, in the case of R_3, the hetero atoms in said heterocycle are not directly bonded to the --CH-- group of the --CH--X-- moiety;

R_2, R_b and R_c are independently selected from carboxy or protected carboxy, carboxy or protected carboxyloweralkyl and carboxyamide;

X is oxygen or nitrogen;

R_4 is H or an amino protecting group; wherein the substituents in the aforementioned substituted alkyl, cycloalkyl, cycloalkylalkyl, amino, acylamino, aryl, aralkyl, aryloxy, alkoxyaryl, alkoxyaryalkyl and heterocyclic groups are selected from the group consisting of halogen, hydroxyl, lower alkyl, lower alkoxy, aryloxy, aralkyloxy, amino, mono- or di-loweralkylamino, arylamino, aralkylamino, carboxyl, formyl, lower alkoxycarbonyl, aryloxycarbonyl, aralkyloxycarbonyl, loweralkylthio, arylthio, aralkylthio, arylsulfinyl, arylsulfinyl, aralkylsulfinyl, lower alkylsulfonyl, arylsulfonyl, aralkylsulfonyl and a monocyclic or bicyclic heterocyclic group having 1- 4 hetero atoms selected from nitrogen, sulfur and oxygen;

or a pharmaceutically acceptable salt thereof.

12. The method according to claim 11, in which the compound of formula I is [R-(R*,R*)]-N-[(R)-6-carboxy-N^2-[[2-carboxy-1-methyl-2-[(1-oxoheptyl)amino]ethoxy] carbonyl]-L-lysyl]-alanine or a pharmaceutically acceptable salt thereof.

13. The method according to claim 12, wherein the microtubular agent or macrphage activating agent is selected from the group consisting of paclitaxcel,

docetaxel, vincristine, vinblastine, vinorelbine, adriamycin, doxirubicin, cisplatin, carboplatin, mitomycin C, and bleomycin.

14. The method according to claim 13, wherein the microtubular agent or macrophage activating agents are paclitaxcel and carboplatin.